REMARKS

Applicants have made minor amendments to claims 2, 4 and 5 to improve readability. Support for the amendments to claim 4 can be found in the originally filed claim 2.

Applicants submit that these amendments do not introduce new issues requiring further search or examination. No new matter is believed to have been added. Claims 1-24 are pending in this application.

I. Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-24 under 35 U.S.C. §103(a) over the combination of *Yang* (US 2005/0053655 A1) and *Ohta* (EP 0914818).

Applicants respectfully submit that the combine references do not support a *prima facie* case of obviousness because they fail to teach all of the limitations of the claimed invention. Furthermore, Applicants submit that the combined references fail to suggest the claimed invention.

The claimed tablet comprises two types of granules compressed together: (a) "rapidly dispersing granules" comprising a "sugar alcohol or a saccharide or a mixture thereof having an average particle size less than about 30 microns", and (b) "taste-masked microcapsules containing at least one drug" prepared by encapsulating a "granulated mass" comprising "at least one drug" *and* "at least one polymeric binder". Applicants further note that granules comprise aggregated "primary" particles.

Yang describes tablets comprising a single type of drug-containing granule, i.e., prepared by dispersing a drug in a hydrogel, hardening the hydrogel coating around the drug particle to form microcapsules, and ultimately granulating the resulting microcapsules to form "microcapsule granules" which are then compressed into an RDT.[1] The presence of other excipients such as disintegrants are "optional"[2], and when combined with the hydrogel coated drug granules, these exipients are in the form of a blend of "primary" particles, not granules.[3] Furthermore, Applicants note that the granulated microcapsules are "wet

[1] e.g., *Yang*, ¶ [0022]
[2] *Yang*, ¶ [0050]
[3] *Yang*, ¶ [0056]

granulated" (i.e., granulated in the presence of a solvent), but not with a "polymeric binder" as in the claimed invention.

Ohta also describes tablets comprising a single type of drug-containing granule, i.e., prepared by granulating together a "sugar alcohol or saccharide", a drug (not taste-masked), and a disintegrant, which are then compressed into an "intraorally" rapidly disintegrating tablet.[4] The "wet granulation" is carried out with "purified water"[5] – i.e., *not* with a polymeric binder as in the claimed invention

Thus, neither cited reference teaches or suggests a tablet comprising two different types of granules compressed into a tablet, one type of granule containing a drug, and the other type of granule containing a disintegrant. In addition, neither cited reference describes a drug-containing granule comprising a polymeric binder. The polymeric binder prevents drug-containing granules from breaking up during coating with a taste-masking layer e.g., by coacervation. Instead, both *Yang* and *Ohta* describe tablets comprising a single type of drug-containing granule lacking a polymeric binder. Thus, the combined references fail to support a *prima facie* case of obviousness because they lack at least two limitations of the claimed invention (i.e., the combination of two separate types of granules, and the presence of a polymeric binder in the drug-containing granule).

The Examiner appears to suggest that one would have been motivated to combine the hydrogel coated granules of *Yang* with sugar alcohol or saccharide granules of *Ohta* to provide the claimed tablets.

However, Applicants respectfully submit that *Yang* and *Ohta* could be combined in many different ways -- many of which would not provide the claimed tablet. For instance, one reasonable combination of *Yang* and *Ohta* would be to simply microencapsulate the granules of *Ohta* with the hydrogel of *Yang*, and compress the resulting coated granules to form a tablet. The resulting tablet would thus comprise a *single* type of granule composed of the drug, sugar or saccharide and disintegrant, which is structurally quite different from the claimed tablet (comprising two different types of granules) and would thus reasonably be expected to have quite different properties (e.g., disintegration, etc.). Alternatively, since *Yang* teaches that e.g., disintegrants are optional, one could also reasonably combine the

[4] e.g., *Ohta*, ¶ [0018], Examples

hydrogel microcapsules of *Yang* with granules of *Ohta*, but modified to exclude the disintegrant and/or the sugar alcohol or saccharide component. Again, the resulting combination would be structurally quite different from the claimed tablet, and reasonably provide a tablet with quite different properties.

Applicants further note that the references themselves do not appear to suggest the very specific selections from *Yang* and *Ohta* required to provide the claimed invention. Rather, Applicants respectfully submit that the specific combination of *Yang* and *Ohta* proposed by the Examiner could reasonably only have been suggested by improper hindsight consideration of Applicant's own application. Accordingly, Applicants respectfully submit that the combination of *Yang* and *Ohta* fails to suggest the claimed invention.

Furthermore, even if *Yang* and *Ohta* were combined as suggested by the Examiner, the combination would not be expected to form the *"taste masked"* microcapsules of the claimed invention. Applicants submit that it is well understood in the pharmaceutical arts that a taste masking coating prevents dissolution of the drug in the mouth during administration of the tablet, thereby preventing the patient from tasting the drug. Such taste masking coatings can be provided by relatively water insoluble polymers such as ethylcellulose.[6]

As discussed above however, only *Yang* discloses a coated drug-containing granule, wherein the coating is a hydrogel. Hydrogels are colloidal gels dispersed in which water (see paragraph [0037] of *Yang*). Hydrogels are well known to comprise mostly water, and the polymer component of the hydrogel is typically quite hydrophilic (see paragraph [0038] of *Yang*). Reasonably, one would expect such a highly hydrated, hydrophilic coating to allow rapid release of the drug in an aqueous environment (e.g., in the mouth), and thus one would not reasonably expect the hydrogel coating of *Yang* to provide taste-masking as required by the present claims. Accordingly, even if *Yang* and *Ohta* were combined in the manner suggested by the Examiner, the resulting combination would still not provide the claimed invention.

With regard to the various pending method claims, Applicants submit that the Examiner has failed to support a *prima facie* case of obviousness. As discussed above,

[5] e.g., *Ohta* ¶ [0023], Examples

neither *Yang* nor *Ohta* disclose preparing two separate granulation steps, blending two separate types of granules, and compressing the blended granules. Furthermore, neither *Yang* nor *Ohta* disclose granulating a drug in the presence of a polymeric binder.

Similarly, there is no specific direction in either reference to combine the methods disclosed therein to provide the claimed method, nor would there be any reasonable motivation to simply combine two separate methods for preparing different types of drug-containing particles.

In view of the foregoing, Applicants respectfully submit that the rejection under 35 U.S.C §103 is improper, and should be withdrawn.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. 1.136(a)(3).

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[6] Present specification, ¶ [0019]